REMARKS

Introductory Comments

Claims 1-16 have been examined in the Office Action under reply and have been variously rejected under (1) 35 U.S.C. §101 for double patenting, as well as under the judicially created doctrine of obviousness-type double patenting; and (2) 35 U.S.C. §102(e), as anticipated. These grounds of rejection are traversed for reasons discussed in detail below.

Overview of the Above Amendments

Claims 2-4, 8, 9, 13, 15 and 16 have been amended to recite the subject invention with greater particularity. Specifically, claims 2, 8, 13 and 15 have been amended to read in independent format and incorporate the recitations of the claims from which they previously depended. These claims further recite a "stock" of recombinant AAV virions produced according to a method comprising, *inter alia*, "introducing an accessory function vector in to the host cell to express accessory functions in the host cell." As explained in the specification at page 14, lines 14-18, an "accessory function vector" refers to a nucleic acid molecule that includes nucleotide sequences providing accessory functions and the term expressly excludes infectious viral particles as they exist in nature, such as adenovirus, herpesvirus or vaccinia virus particles. Thus, a stock of recombinant virions produced according to the recited methods is free of adenovirus and herpesvirus.

The dependent claims have been amended to track the working of the independent claims and to depend from pending rather than canceled claims.

Support for these amendments may be found in the claims as originally filed, as well as throughout the specification at, e.g., page 9, line 12 and page 14, lines 14-18.

Claims 1, 5-7, 10-12 and 14 have been canceled in order to hasten prosecution. Cancellation of these claims is without prejudice, without intent to abandon any originally claimed subject matter, and without intent to acquiesce in any rejection of record. Applicant expressly reserves the right to file one or more continuing applications hereof containing these canceled claims.

The Double Patenting Rejections:

Claims 1, 3-7, 9-12, 14 and 16 were rejected under 35 U.S.C. §101 as claiming the same invention as claims 1-12 of U.S. Patent No. 6,027,931. Additionally, claims 5 and 6 were rejected under 35 U.S.C. §101 as claiming the same invention as claims 1 and 2 of U.S. Patent No. 6,365,403. As explained above, claims 1, 5-7, 10-12 and 14 have been canceled. Claims 3, 4, 9 and 16 now depend from claim 2 (claims 3 and 4), claim 8 (claim 9) and claim 15 (claim 16) which claims were not subject to the rejection. Thus, the double patenting rejection under 35 U.S.C. §101 has been overcome. Withdrawal thereof is respectfully requested.

Claims 2, 8, 13 and 15 were rejected under the judicially created doctrine of obviousness-type double patenting over claims 1-12 of U.S. Patent No. 6,027,931. Applicants disagree with this rejection vis-a-vis the present claims. In particular, as explained above, all of the current claims recite a stock of recombinant AAV virions produced using an accessory function vector to express accessory functions in the host cell in order to produce a stock that lacks adenovirus and herpesvirus. Claims 1-12 of U.S. Patent 6,027,931 pertain to methods and host cells and are not limited to the use of accessory function vectors. Accordingly, applicants believe the present claims should not be subject to the rejection and request withdrawal thereof.

Claims 12 and 14 were rejected under the judicially created doctrine of obviousness-type double patenting over claims 7-10 of U.S. Patent No. 6,365,403.

Claims 12 and 14 have been canceled, rendering this rejection moot. Withdrawal thereof is respectfully requested.

35 U.S.C. § 102(e):

Claims 2, 8, 13 and 14 were rejected under 35 U.S.C. §102(e) as anticipated by U.S. Patent No. 5,436,146 to Shenk et al. The Office argues:

> Shenk et al. claim a 'helper free stock of rAAV (claim 12) generated with a recombinant helper AAV DNA in combination with a rAAV vector comprised of up to 195 base pairs of the AAV ITRs...While the rAAV of Shenk et al is produced by slightly different methods from that of the instant application; the resulting product, absent evidence to the contrary, does not differ from that in Shenk et al.

Office Action, page 5. However, applicants respectfully disagree that the present claims are anticipated by Shenk.

In particular, all of the current claims pertain to stocks of recombinant AAV virions produced using accessory function vectors. As explained above and in the specification, accessory function vectors provide accessory functions in the absence of infectious virus. Accordingly, the resultant stock of virions is free from adenovirus and herpesvirus. Shenk, on the other hand, only describes production of recombinant AAV virions in the presence of infectious viruses such as adenovirus or herpesvirus. Stocks produced in this manner would therefore not be devoid of adenovirus and herpesvirus.

Thus, applicants' stocks are fundamentally different compositions than those of the cited art. Accordingly, withdrawal of the rejections over the art is respectfully requested.

CONCLUSION

In view of the foregoing, applicant submits that the claims are now in condition for allowance and request early notification to that effect. If the Examiner notes any further matters which she believes may be resolved by a telephone interview, she is encouraged to contact Christina Thomson by telephone at (510)748-7208, or by fax at (510)748-7155.

Respectfully submitted,

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Version with markings to show changes made

In the Claims:

The claims have been amended as follows:

1. CANCELED

2. (Amended) A stock of recombinant AAV [virion] virions produced according to [the] a method [of claim 1] comprising:

(a) introducing an AAV vector into a host cell;

(b) introducing an AAV helper function vector comprising an AAV *rep* coding region into the host cell, wherein said *rep* coding region comprises a nucleotide sequence coding for long forms of Rep protein and short forms of Rep protein, such that the host cell produces greater quantities of the short forms of Rep protein than of the long forms of Rep protein;

(c) introducing an accessory function vector into the host cell to express accessory functions in the host cell; and

(d) culturing the host cell to produce a stock of recombinant AAV virions free of adenovirus and herpesvirus.

3. (Amended) The [method] stock of claim [1] 2, wherein the AAV helper function vector further comprises an AAV *cap* coding region.

4. (Amended) The [method] stock of claim [1] 2, wherein the host cell produces at least ten-fold greater quantities of the short forms of Rep protein than of the long forms of Rep protein.

5. CANCELED.

6. CANCELED.

7. CANCELED

8. (Amended) A stock of recombinant AAV [virion] virions produced according to [the] a method [of claim 7] comprising:

(a) introducing an AAV vector into a host cell;

(b) introducing an AAV helper function vector comprising an AAV *rep* coding region into the host cell, wherein said *rep* coding region comprises a nucleotide sequence coding for long forms of Rep protein and short forms of Rep protein, and said AAV helper function vector causes the host cell to produce an amount of the long forms of Rep protein that is substantially less than an amount produced from an AAV helper function vector expressing the long forms of Rep protein under control of an AAV p5 promoter;

(c) introducing an accessory function vector into the host cell to express accessory functions in the host cell; and

(d) culturing the host cell to produce a stock of recombinant AAV virions free of adenovirus and herpesvirus.

9. (Amended) The [method] stock of claim [7] 8, wherein the AAV helper function vector further comprises an AAV *cap* coding region.

10. CANCELED

11. CANCELED

12. CANCELED

13. (Amended) A stock of recombinant AAV [virion] virions produced according to [the] a method [of claim 12] comprising:

(a) introducing an AAV vector into a host cell;

(b) introducing an AAV helper function vector comprising AAV *rep* and *cap* coding regions into the host cell to express Rep and Cap gene products, wherein the *rep* coding region is under the control of an inducible promoter that expresses an amount of *rep* RNA that is substantially less than an amount expressed from an AAV p5 promoter;

(c) introducing an accessory function vector into the host cell to express accessory functions in the host cell; and

(d) culturing the host cell to produce a stock of recombinant AAV virions free of adenovirus and herpesvirus.

14. CANCELED.

15. (Amended) A stock of recombinant AAV [virion] virions produced according to [the] a method [of claim 14] comprising:

(a) introducing an AAV vector into a host cell;

(b) introducing an AAV helper construct comprising AAV *rep* and *cap* coding regions into the host cell to express Rep and Cap gene products, wherein said *rep* coding region comprising a nucleotide sequence coding for long forms of Rep protein and short forms of Rep protein, wherein the *rep* coding region is regulated by an inducible promoter such that the host cell produces greater quantities of the short forms of Rep protein than of the long forms of Rep protein;

(c) introducing an accessory function vector into the host cell to

express accessory functions in the host cell; and

(d) culturing the host cell to produce a stock of recombinant AAV virions free of adenovirus and herpesvirus.

16. (Amended) The [method] stock of claim [14] 15, wherein the host cell produces at least ten-fold greater quantities of the short forms of Rep protein than of the long forms of Rep protein.

Currently Pending Claims

2. (Amended) A stock of recombinant AAV virions produced according to a method comprising:

(a) introducing an AAV vector into a host cell;

(b) introducing an AAV helper function vector comprising an AAV *rep* coding region into the host cell, wherein said *rep* coding region comprises a nucleotide sequence coding for long forms of Rep protein and short forms of Rep protein, such that the host cell produces greater quantities of the short forms of Rep protein than of the long forms of Rep protein;

(c) introducing an accessory function vector into the host cell to express accessory functions in the host cell; and

(d) culturing the host cell to produce a stock of recombinant AAV virions free of adenovirus and herpesvirus.

3. (Amended) The stock of claim 2, wherein the AAV helper function vector further comprises an AAV *cap* coding region.

4. (Amended) The stock of claim 2, wherein the host cell produces at least ten-fold greater quantities of the short forms of Rep protein than of the long forms of Rep protein.

8. (Amended) A stock of recombinant AAV virions produced according to a method comprising:

(a) introducing an AAV vector into a host cell;

(b) introducing an AAV helper function vector comprising an AAV *rep*

coding region into the host cell, wherein said *rep* coding region comprises a nucleotide sequence coding for long forms of Rep protein and short forms of Rep protein, and said AAV helper function vector causes the host cell to produce an amount of the long forms of Rep protein that is substantially less than an amount produced from an AAV helper function vector expressing the long forms of Rep protein under control of an AAV p5 promoter;

(c) introducing an accessory function vector into the host cell to express accessory functions in the host cell; and

(d) culturing the host cell to produce a stock of recombinant AAV virions free of adenovirus and herpesvirus.

9. (Amended) The stock of claim 8, wherein the AAV helper function vector further comprises an AAV *cap* coding region.

13. (Amended) A stock of recombinant AAV virions produced according to a method comprising:

(a) introducing an AAV vector into a host cell;

(b) introducing an AAV helper function vector comprising AAV *rep* and *cap* coding regions into the host cell to express Rep and Cap gene products, wherein the *rep* coding region is under the control of an inducible promoter that expresses an amount of *rep* RNA that is substantially less than an amount expressed from an AAV p5 promoter;

(c) introducing an accessory function vector into the host cell to express accessory functions in the host cell; and

(d) culturing the host cell to produce a stock of recombinant AAV virions free of adenovirus and herpesvirus.

15. (Amended) A stock of recombinant AAV virions produced according to a method comprising:

(a) introducing an AAV vector into a host cell;

(b) introducing an AAV helper construct comprising AAV *rep* and *cap* coding regions into the host cell to express Rep and Cap gene products, wherein said *rep* coding region comprising a nucleotide sequence coding for long forms of Rep protein and short forms of Rep protein, wherein the *rep* coding region is regulated by an inducible promoter such that the host cell produces greater quantities of the short forms of Rep protein than of the long forms of Rep protein;

(c) introducing an accessory function vector into the host cell to express accessory functions in the host cell; and

(d) culturing the host cell to produce a stock of recombinant AAV virions free of adenovirus and herpesvirus.

16. (Amended) The stock of claim 15, wherein the host cell produces at least ten-fold greater quantities of the short forms of Rep protein than of the long forms of Rep protein.